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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/559,783	12/08/2005	Mitsuko Kosaka	64614(70904)	1080

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EXAMINER	
DUTT, ADITI	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/559,783	KOSAKA, MITSUKO	
	Examiner	Art Unit	
	Aditi Dutt	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,8-14,17,18,26 and 27* is/are pending in the application.

4a) Of the above claim(s) *12-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,8-11,17-18,26-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. The amendments filed on 25 April 2008 have been entered into the record and have been fully considered. Claims 5 and 19-25 are cancelled. Claims 1 and 6 are amended. New claims 26-27 are added.

2. Claims 1-4, 6, 8-11, 17-18 and 26-27 drawn to a method for producing myocardial tissue cells culturing iris pigment epithelial cells and obtaining pluripotent cells therefrom, are under consideration in the instant application.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicants response and withdrawn.

4. Applicant's arguments filed on 25 April 2008, have been fully considered. New grounds of objection and rejection are as follow.

Response to Amendment

Withdrawn objections and/or rejections

5. Upon consideration of the Applicant's amendment, all claim objections and rejections, not reiterated herein have been withdrawn, as overcome by cancellation and/or amendment of claims (25 April 2008).

6. Rejection of claims 20 and 22, under 35 U.S.C. 112, second paragraph is withdrawn because of cancellation of the claims.

7. Rejection of claims 19-21, 23-25, under 35 U.S.C. 112, written description is withdrawn because of cancellation of the claims.

8. Rejection of claims 1-6, 8-11 and 17-18, under 35 U.S.C. 103(a), is withdrawn because of amendment of independent claims 1 and 6.

New grounds of claim rejections/objections

Claim Objections

9. Claim1 is objected to because of the following informalities: Claim 1, step (v) recites "one or more types of tissue cells" instead of "myocardial cells". Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1-4, 6, 8-11, 17- 18, and 26-27 are rejected under 35 U.S.C.103(a) as being unpatentable over Kosaka et al. (Exp Cell Res 245: 245-251, 1998), and Haruta et al., (Nat Neurosc 4: 1163-1164, 2001); in view of Rezai et al. (Investig Opthal Vis Sci 38: 2255-2260, 1997).

11. The claims are drawn to a method for producing myocardial tissue cells comprising: (i) an iris-tissue-extirpating step from an eyeball of a postnatal animal, for example, chicken, mouse, rat or human, by enzyme treatment (dispase followed with EDTA, and restoration of the iris by treating with FCS) (claims 1-3, 6, 26-27); (ii) separating the iris pigment epithelium (IPE) from the extirpated iris tissue; (iii) dissociating IPE using trypsin solution; (iv) obtaining pluripotent stem cells by selectively culturing epithelial cells by floated coagulated mass culturing technique to obtain pluripotent stem cells, that are Oct-3/4 positive, and/or tridermic differentiable (claim 1, 4); (v) obtaining tissue cells by culturing pluripotent stem cells under differentiation inducing conditions comprising culture of the cells in the presence of serum (fetal calf or avian) with a growth factor (FGF or EGF) (claims 8-11). Furthermore, the claims recite testing for the expression of one gene selected from GATA4, Nkx2.5, myosin etc. specific for myocardial cells (claims 17 and 18).

12. Kosaka et al. teach the removal of eyeballs from 1 day old (postnatal) chicken, followed by incision around the iris, incubating the tissue in dispase solution and thereafter in EDTA (page 246, col 1, para 3),mechanically isolating the pigmented epithelial cells from the iris so as to prevent contamination with the other cell types, and culture in EF medium containing fetal bovine serum. Isolated epithelia are thereafter dissociated into a single cell suspension after treatment with 0.1% trypsin in PBS (page 246, column 1, "Preparation of cell"). Kosaka et al. further teach the growth of the iris derived pigmented epithelial cells

in culture in EF medium for 18 days before reaching confluency. The depigmented iris pigment epithelial cells are harvested and cultured for transdifferentiation to lens tissue (page 246, column 1, "Procedure for cell culture").

13. Kosaka et al. do not teach the presence of EGF or FGF for differentiation.

14. Haruta et al. teach the differentiation of iris-derived cells (from adult rats) to rod photoreceptor (page 1163, column 2, para 1), in response to *Crx* gene transfer. Haruta et al. further teach the differentiation inducing culture conditions comprising culturing in the presence of 1% fetal bovine serum with 10ng/ml FGF, as growth factor.

15. Kosaka et al. and Haruta et al. do not teach the culturing of iris pigment epithelium cells by a floated coagulated mass culturing technique.

16. Rezai et al. teach culturing of iris pigment epithelial cells from porcine eyes. Specifically, Rezai et al. teach the removal of eyeballs, followed by excision of the iris from the eyeball, incubating the tissue in trypsin-EDTA solution containing growth medium and fetal bovine serum. Furthermore, iris pigmented epithelial cells were isolated from the stroma, incubated in growth medium, and cultured for 7 to 10 days to form spheres (page 2256, "Isolation and culture"), that are three-dimensional cell aggregates which can be easily aspirated and ransferred from one plate to another, therefore, are inherently in suspension or floating (page 2259, col 2, para 2). Furthermore, the spheroid model is

particularly preferred because of its "highly proliferative activity and resistance to dedifferentiation"(page 2255, para 1).

17. Kosaka et al., Haruta et al., and Rezai et al, do not explicitly teach the expression of Oct3/4. However, this limitation will be an inherent feature since the combined references teach the eyeball as the source, follow the same method steps for separating and maintaining iris pigment epithelial cells, followed by the floated mass culture technique, under the same culture limitations of the instant application. Additionally, since the cells of Kosaka et al. and Haruta et al are derived from the same source as the instant application, are cultured under similar differentiation conditions, the three inherently display the same differentiation properties, and express similar marker, absent evidence to the contrary. That the references are silent on the expression of the cardiac marker genes does not provide proof of the cell being different, particularly if the other conditions (as stated above) are satisfied.

18. It would have been, therefore, obvious to the person of ordinary skill in the art at the time the claimed invention was made to modify the method of culturing the iris pigment epithelial cells of Kosaka et al. and Haruta et al., to the floated coagulated mass culture technique as taught by Rezai et al. The person of ordinary skill in the art would have been motivated to use the spheroid model for cell culture as direct cell-to-cell contact may provide the regulatory signals for IPE cells to induce proliferation or differentiation (Rezai et al., page 2259, col 2). The person of ordinary skill in the art would have expected success because the

method of floated coagulated mass technique, was well established and accepted in the art at the time the invention was made.

19. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

20. No claims are allowed.

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

22. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose telephone number is (571) 272-9037. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:00 p.m.

24. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

25. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov/. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AD
12 August 2008

/Jeffrey Stucker/

Supervisory Patent Examiner, Art Unit 1649